haematocrit, white cell count (WCC)) in 64 patients (43 male; mean age 63.2 years, s.d. 8.9) admitted with acute stroke (ictus onset < 12 hours). Levels of these markers and blood pressures (BPs, mmHg) were compared to 21 healthy controls (age 61.5 years, s.d. 11.7). Our results are shown in the table.

There were no significant differences in these markers and BPs between patients who were alive or dead (n = 13) after 6 months followup. Plasma viscosity was sinificantly correlated to fibrinogen ($r = 0.5, p < 0.001$) and vWf ($r = 0.3$, $p = 0.04$). Stepwise multiple regression analysis demonstrated that fibrinogen and diastolic BPs were predictors for plasma viscosity ($p = 0.018$). Only the WCC level was a predictor for fibrinogen levels ($p = 0.03$). There were no significant predictors for vWf and P-selectin levels. Despite early presentation (< 12 hours) patients with acute stroke have haemorheological abnormalities (fibrinogen, WCC and plasma viscosity), platelet dysfunction (with raised P-selectin) and endothelial dysfunction (with high vWf). These abnormalities may act synergistically in the pathogenesis of acute stroke and its complications.

SUNDAY POSTER

PHARMACOLOGY – BASIC

901-112 Two Intracoronary Doses of Basic Fibroblast Growth Factor Enhance Collateral Blood Flow in Dogs

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Basic fibroblast growth factor (bFGF), an angiogenic growth factor, is currently the subject of a Phase I clinical trial in pts with ischemic heart disease (IHD). In a canine model of single vessel coronary occlusion, we previously demonstrated that bFGF enhances collateral blood flow (CBF) when given as a daily I.C. bolus for 4 weeks, or as a daily left atrial bolus for 7 days; however, these schedules and routes of administration would not be practical in pts with IHD. To establish a feasible route of drug delivery and to limit potential systemic toxicity, we determined whether injection of bFGF into the left main coronary artery would enhance CBF. A second aim was to establish the minimum effective course of bFGF treatment. Dogs were subjected to ameroid-induced occlusion of the left circumflex coronary artery. Subsequently, the dogs underwent cardiac catheterization and were randomized to receive bFGF 0.1 mg/kg as a bolus into the left main coronary artery twice (14 and 16 days after ameroid placement, $n = 10$) or once (day 16, $n = 8$). A control group received the vehicle ($n = 10$). CBF was assessed during maximal coronary vasodilatation with radiolabeled microspheres on day 33. Maximal CBF in dogs that received bFGF twice was 2.39 ± 0.09 ml/min/g, exceeding that of control dogs by 39% (1.72 ± 0.13 ml/min/g, mean $\pm$ SE; $P < 0.0005$). Dogs that received a single dose of bFGF had an intermediate flow (2.10 ± 0.21), statistically indistinguishable from the other groups. Thus, two doses of bFGF administered into the left main coronary artery were sufficient to improve CBF, an intervention that is feasible in pts with IHD. These data provide the basis for a trial of intracoronary bFGF in pts with IHD.

901-113 Effects of Mac-1 Inhibitor on Hemostasis During Myocardial Stunning in Swine

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The important role of hemostatic disorders has been increasingly recognized in patients with myocardial ischemia. NPC 15669 is a member of the leumedins, and inhibits leukocyte adhesion to the endothelium by blockage of Mac-1 upregulation. The effects of NPC 15669 supplementation on the hemostatic profile during myocardial stunning (MS) are poorly understood. Thus, the purpose of this project was to link potential changes in hemostatic profile with NPC 15669 therapy during mild MS in *in vivo* animal model.

Twelve open-chested Yorkshire swine underwent LAD occlusion for 8 minutes followed by 90 minutes of reperfusion. Blood samples were obtained at baseline, at 4 and at 8 minutes of occlusion, and at 60 and 90 minutes of reperfusion. NPC 15669 (10 mg/kg loading dose followed by constant infusion at 6 $mg/kg^{-1}/h^{-1}$) was administered in 6 animals; another 6 swine received saline and served as controls. Concentrations of antithrombin-III (AT-III), Protein C, total Protein S, fibronectin, endothelin-1 (ET-1), as well as the stable metabolites of thromboxane (TxB_2) and prostacyclin (6-keto-PGF_{1a}), were measured in the systemic circulation. Treatment with NPC 15669 was associated with diminished ET-1 (37.4%), 6-keto-PGF_{1a} (47.1%) levels and increased fibronectin (77.6%) concentrations during MS. There were no changes in the plasma concentrations of TxB_2, total protein S, protein C and AT-III in NPC 15669 group when compared with controls.

Mild MS is associated with substantial dynamic changes in the hemostatic profile. NPC 15669 administration in a swine model of MS affects specific hemostatic parameters. This data provides strong support for the involvement of cellular mechanisms and endothelial dysfunction in the pathogenesis of MS. The ability of the drug to modulate hemostasis may have implications for the use of leumedins in cardiovascular disease.

PHARMACOLOGY – CLINICAL

901-114 Effect of Calcium Channel Blockers on the Incidence of Myocardial Infarction in Patients With Left Ventricular Dysfunction

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Recent studies have suggested an increased risk of myocardial infarction (MI) in patients on calcium channel blockers (CCB). We evaluated the effect of CCB on fatal and non-fatal MI in 6797 patients with left ventricular dysfunction (LVD, EF $\leq$ 35%) in the Studies Of Left Ventricular Dysfunction (SOLVD).

During 40 months average follow-up, fatal or non-fatal MI occurred in 11.5% of the 845 patients on CCB during follow-up versus 7.5% of the 2551 patients not on CCB ($p = 0.001$, O.R. 1.6; 95% CI 1.24–2.07) in the enalapril group; and in 14.4% of the 874 patients on CCB versus 9.3% of the 2527 patients not on CCB ($p = 0.001$, O.R. 1.64; CI 1.30–2.06) in the placebo group.

By multivariate Cox regression analysis, adjusting for 29 variables describing demographics, comorbidity, etiology and severity of LVD, heart failure, and concomitant drug use, CCB use during follow-up was an independent predictor of increased risk (R.R. 1.37; CI 1.14–1.63).

The increased risk associated with CCB was also observed when the combined endpoint of MI, cardiac death, or hospitalization for angina was considered. The incrcased MI risk was observed whether CCB were used both at baseline and follow-up or only at follow-up. In addition, the risk was higher when the mean follow-up heart rate of patients on CCB was higher than the median follow-up rate of patients on CCB (74 beats/minute).

In contrast, using the same database and analysis, beta blocker use was associated with a lower rate of fatal or non-fatal MI (multivariate Cox R.R. 0.80; CI 0.61–1.05).

In this retrospective analysis of patients with LVD, CCB use was associated with significantly increased risk of MI.

901-115 Is Thrombolytic Therapy Most Effective When Endogenous Fibrinolysis Is Deficient?

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Thrombi that form as a result of defective endogenous fibrinolysis may be most sensitive to thrombolytic agents. Impaired fibrinolytic activity has been associated with low plasma levels of single-chain urokinase (scu-PA), raised lipoprotein(a) [Lp(a)] and, paradoxically, high t-PA antigen.

We investigated the relation between endogenous fibrinolytic factors on admission and subsequent efficacy of thrombolytic therapy in 51 patients with acute myocardial infarction (AMI) treated within 6 h of symptoms with intravenous rt-PA (20–60 MU) and heparin. Pre-treatment plasma concentrations of Lp(a) (mg/dl), t-PA antigen (ug/L) and urokinase (u-PA, ug/L) were measured by ELISAs and of scu-PA (ug/L) by bioimmunoassay. A coronary arteriogram was performed 90 min after the start of lytic therapy. Perfusion of the infarct-artery was defined as TIMI grade 3.

At 90 min, a TIMI 3 infarct-artery was found in 27 pts. The perfused vs occluded-artery pts did not differ significantly in age, sex, smoking status, delay to treatment, time of day of therapy or rt-PA dose at 90 min. Plasma factors (median and interquartiles) were:

	Lp(a)	t-PA	scu-PA	u-PA
Perfused	16 (11–32)	26 (17–39)	1.9 (1.6–2.1)	2.7 (2.2–3)
Occluded	9 (5–27)	15 (10–21)	2.1(1.9–2.6)	2.6 (2.4–2.8)
p value	0.02	0.003	0.03	0.38

Thus, in patients with AMI receiving rt-PA, early coronary reperfusion, compared with persistent occlusion, is associated with higher plasma Lp(a) and t-PA antigen levels and lower plasma scu-PA on admission. Pharmacological doses of rt-PA thus appear most effective when natural fibrinolysis is deficient.

901-116 Effect of Prostacyclin Infusion as a Treatment of Pulmonary Hypertension

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We have examined the effect of continuous infusion of prostacyclin (PGI_2)